Performance of doubly-robust, machine learning effect estimators in realistic epidemiologic data settings and practical recommendations.

# Background

Flexible, data-adaptive algorithms (machine learning; ML) for nuisance parameter estimation in epidemiologic causal inference have promising high-dimensional and asymptotic properties. However, recently proposed applications (*e.g*. targeted maximum likelihood estimation; TMLE) may be biased and anticonservative at sample sizes (N <2000) and covariate dimensions common to measurement-intensive longitudinal cohorts. The relative benefit of non-parametric ML over simpler regression-based approaches in such settings is unclear.

# Methods

I evaluate bias and variance estimation using cross-validated TMLE, augmented inverse probability weighting (AIPW), and standard IPW in fully parametrically-simulated datasets of sizes N = 200 to 2000 and structure-preserving (“plasmode”) simulations of 1,174 subjects (331 covariates) from a longitudinal birth cohort.

# Results

Performance of TMLE, AIPW, and IPW were acceptable (bias: 0.1% to 3.9% of true effect; coverage: 91% to 96%) when parametric learners (GLM, elastic net, polynomial splines) were used. However, non-parametric algorithms (boosted regression trees, random forests) led to substantial bias (>45%) and poor coverage (<46%), with AIPW consistently outperforming TMLE. In high-dimensional plasmode datasets where standard IPW fails, non-parametric slightly outperformed parametric algorithms (bias: 1.7% vs. 2.0%).

# Conclusions

At small sample sizes, non-parametric ML may have worse performance than simpler models, even when ensembled and cross-validated. Estimates from such algorithms should be compared using simpler estimators and performance evaluated by simulation.

# Key messages

In smaller epidemiologic studies, use of machine learning for effect estimation should be strongly justified (*i.e*. high-dimensional covariates) and performed with care. Smooth, parametric learners may be a safe option with few drawbacks.